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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Complete if Known

Application Number	10/783,780
Filing Date	02/20/2004
First Named Inventor	Abeliovich, Asa
Art Unit	1646 1633
Examiner Name	
Attorney Docket Number	5199/70

Sheet 1 of 2

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
SK	1	Alves-Rodrigues et al., Ubiquitin, cellular inclusions and their role in neurodegeneration. Trends Neurosci., 21:516-20, 1998	
	2	Burke and Kholodilov, Programmed cell death: does it play a role in Parkinson's disease? Ann. Neurol., 44:S126-33, 1998	
	3	Carrano et al., SKP2 is required for ubiquitin-mediated degradation of the CDK inhibitor p27. Nat. Cell Biol., 1:193-99, 1999	
	4	Chung et al., Parkin ubiquitinates the alpha-synuclein-interacting protein, synphilin-1: implications for Lewy-body formation in Parkinson disease. Nat. Med., 7:1144-50, 2001	
	5	Chung et al., The role of the ubiquitin-proteasomal pathway in Parkinson's disease and other neurodegenerative disorders. Trends Neurosci., 24:S7-14, 2001	
	6	Clurman et al., Turnover of cyclin E by the ubiquitin-proteasome pathway is regulated by cdk2 binding and cyclin phosphorylation. Genes Dev., 10:1979-90, 1996	
	7	Dealy et al., Loss of Cul1 results in early embryonic lethality and dysregulation of cyclin E. Nat. Genet., 23:245-48, 1999	
	8	Dong et al., ebi regulates epidermal growth factor receptor signaling pathways in Drosophila. Genes Dev., 13:954-65, 1999	
	9	Ekholm and Reed, Regulation of G(1) cyclin-dependent kinases in the mammalian cell cycle. Curr. Opin. Cell Biol., 12:676-84, 2000	
SK	10	Elbashir et al., Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells. Nature, 411:494-98, 2001	

Examiner Signature	/Sumesh Kaushal/ (08/16/2006)	Date Considered	
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	12	Fallon et al., Parkin and CASK/LIN-2 associate via a PDZ-mediated interaction and are co-localized in lipid rafts and postsynaptic densities in brain. J. Biol. Chem., 25:25, 2001	
	13	Hershko et al., Components of ubiquitin-protein ligase system. Resolution, affinity purification, and role in protein breakdown. J. Biol. Chem., 258:8206-14, 1983	
	14	Husseman et al., Mitotic activation: a convergent mechanism for a cohort of neurodegenerative diseases Neurobiol. Aging, 21:815-28, 2000	
	15	Hynes et al., Induction of midbrain dopaminergic neurons by Sonic hedgehog. Neuron, 15:35-44, 1995	
	16	Imai et al., An unfolded putative transmembrane polypeptide, which can lead to endoplasmic reticulum stress, is a substrate of Parkin. Cell, 105:891-02, 2001	
	17	Imai et al., CHIP is associated with parkin, a gene responsible for familial Parkinson's disease, and enhances its ubiquitin ligase activity. Mol. Cell., 10:55-67, 2002	
	18	Imai et al., Parkin suppresses unfolded protein stress-induced cell death through its E3 ubiquitin-protein ligase activity. J. Biol. Chem., 275(46):35661-664, 2000	
	19	Joazeiro and Weissman, RING finger proteins: mediators of ubiquitin ligase activity. Cell, 102:549-52, 2000	
SK	20	Kamura et al., Rbx1, a component of the VHL tumor suppressor complex and SCF ubiquitin ligase. Science, 284:657-61, 1999	

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SK	21	Kitada et al., Mutations in the parkin gene cause autosomal recessive juvenile parkinsonism. Nature, 392:605-08, 1998	
	22	Klein et al., The harlequin mouse mutation downregulates apoptosis-inducing factor. Nature, 419:367-74, 2002	
	23	Koepp et al., Phosphorylation-dependent ubiquitination of cyclin E by the SCFFbw7 ubiquitin ligase. Science, 294:173-77, 2001	
	24	Krichevsky and Kosik, RNAi functions in cultured mammalian neurons. Proc. Natl Acad. Sci. USA, 99:11926-929, 2002	
	25	Kubo et al., Parkin is associated with cellular vesicles. J. Neurochem., 78:42-54, 2001	
	26	Lang and Lozano, Parkinson's disease. First of two parts. N. Engl. J. Med., 339:1044-53, 1998	
	27	Leroy et al., The ubiquitin pathway in Parkinson's disease. Nature, 395:451-52, 1998	
	28	Liu and Greene, Neuronal apoptosis at the G1/S cell cycle checkpoint. Cell Tissue Res., 305:217-28, 2001	
	29	Lotharius et al., Distinct mechanisms underlie neurotoxin-mediated cell death in cultured dopaminergic neurons. J. Neurosci., 19:1284-93, 1999	
SK	30	Matsuzawa and Reed, Siah-1, SIP, and Ebi collaborate in a novel pathway for beta-catenin degradation linked to p53 responses. Mol. Cell, 7:915-26, 2001	

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SK	31	Moberg et al., Archipelago regulates Cyclin E levels in Drosophila and is mutated in human cancer cell lines. Nature, 413:311-16, 2001	
	32	Neystat et al., Expression of cyclin-dependent kinase 5 and its activator p35 in models of induced apoptotic death in neurons of the substantia nigra in vivo. J. Neurochem., 77:1611-25, 2001	
	33	Nirenberg et al., The dopamine transporter is localized to dendritic and axonal plasma membranes of nigrostriatal dopaminergic neurons. J. Neurosci., 16:436-47, 1996	
	34	Olanow and Tatton, Etiology and pathogenesis of Parkinson's disease. Annu. Rev. Neurosci., 22 :123-44, 1999	
	35	Padmanabhan et al., Role of cell cycle regulatory proteins in cerebellar granule neuron apoptosis. J. Neurosci., 19:8747-56, 1999	
	36	Park et al., Cyclin-dependent kinases participate in death of neurons evoked by DNA- damaging agents. J. Cell Biol., 143:457-67, 1998	
	37	Patton et al., Combinatorial control in ubiquitin-dependent proteolysis: don't Skp the F-box hypothesis. Trends Genet., 14:236-43, 1998	
	38	Petrucelli et al., Parkin protects against the toxicity associated with mutant alpha-synuclein: proteasome dysfunction selectively affects catecholaminergic neurons. Neuron, 36: 1007-19, 2002	
	39	Polymeropoulos et al., Mutation in the alpha-synuclein gene identified in families with Parkinson's disease. Science, 276:2045-47, 1997	
SK	40	Raina et al., Cyclin' toward dementia: cell cycle abnormalities and abortive oncogenesis in Alzheimer disease. J. Neurosci. Res., 61:128-33, 2000	

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SK	41	Scheiffele et al., Neuroligin expressed in nonneuronal cells triggers presynaptic development in contacting axons. Cell, 101:657-69, 2000	
	42	Schlossmacher et al., Parkin localizes to the Lewy bodies of Parkinson disease and dementia with Lewy bodies. Am. J. Pathol., 160:1655-67, 2002	
	43	Shimura et al., Familial Parkinson disease gene product, parkin, is a ubiquitin-protein ligase. Nat. Genet., 25:302-05, 2000	
	44	Shimura et al., Ubiquitination of a new form of alpha-synuclein by parkin from human brain: implications for Parkinson's disease. Science, 293:263-69, 2001	
	45	Singer et al., Cullin-3 targets cyclin E for ubiquitination and controls S phase in mammalian cells. Genes Dev., 13:2375-87, 1999	
	46	Skowyra et al., F-box proteins are receptors that recruit phosphorylated substrates to the SCF ubiquitin-ligase complex. Cell, 91: 9-19, 1997	
	47	Skowyra et al., Reconstitution of G1 cyclin ubiquitination with complexes containing SCFGrr1 and Rbx1. Science, 284:662-65, 1999	
	48	Spillantini et al., Alpha-synuclein in Lewy bodies. Nature, 388:839-40, 1997	
	49	Strohmaier et al., Human F-box protein hCdc4 targets cyclin E for proteolysis and is mutated in a breast cancer cell line. Nature, 413:316-22, 2001	
SK	50	Takada et al., Protection against dopaminergic nigrostriatal cell death by excitatory input ablation. Eur. J. Neurosci., 12:1771-80, 2000	

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	52	Verdaguer et al., Kainic acid-induced apoptosis in cerebellar granule neurons: an attempt at cell cycle re-entry. Neuroreport, 13:413-16, 2002	
	53	Winston et al., Culprits in the degradation of cyclin E apprehended. Genes Dev., 13:2751-57, 1999	
	54	Wu et al., Evidence for functional and physical association between Caenorhabditis elegans SEL-10, a Cdc4p-related protein, and SEL-12 presenilin. Proc. Natl Acad. Sci. USA, 95:15787-791, 1998	
	55	Wu et al., SEL-10 is an inhibitor of Notch signaling that targets Notch for ubiquitin-mediated protein degradation. Mol. Cell Biol., 21:7403-15, 2001) and presenilin	
	56	Zennou et al., The HIV-1 DNA flap stimulates HIV vector-mediated cell transduction in the brain. Nat. Biotechnol., 19:446-50, 2001	
	57	Zhang et al., Parkin functions as an E2-dependent ubiquitin- protein ligase and promotes the degradation of the synaptic vesicle-associated protein, CDCrel-1. Proc. Natl Acad. Sci. USA, 97:13354-359,	
	58	Bodansky, M., Principles of Peptide Synthesis (New York: Springer-Verlag New York, Inc., 1984 - (Not Available)	
SK	59	Modern Techniques of Peptide and Amino Acid Analysis (New York: John Wiley & Sons, 1981 - (Not Available)	

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